NTP
National Toxicology Program

1-Chloro-4-(trifluoromethyl)benzene (PCBTF) Research Concept

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PCBTF Nomination

- Nominated for toxicological testing by a representative from Kowa American Corporation (an importer)
  - Lack of OSHA, NIOSH or ACGIH exposure limits
  - Expanded use and greater potential for exposure to workers and general public
- Request by public commenter for NTP to evaluate existing toxicity data and determine need for chronic testing
  - Increasing use as a volatile organic compound exempt solvent in automobile body coatings and parts cleaning
- Recommended for chronic toxicity, reproductive toxicity and carcinogenicity studies

PCBTF Background

- Production
  - No longer produced in US
  - 1-10 million pounds imported (2005)
- Use
  - Non ozone-depleting solvent in paint and coating formulations
  - Intermediate in the synthesis of other compounds, including herbicides
- Human Exposure
  - Most likely exposures are via inhalation in occupational settings
  - Change from intermediate to end user applications with relatively high exposure potential
  - Some reports of occurrence in environmental media (air, water, soil)

PCBTF Toxicity

- Low acute toxicity
- Subacute oral (rats and mice) and subchronic inhalation (rats) toxicity data available
- Primary target organs include the liver and kidney
- Cytotoxic but not genotoxic to bacterial and mammalian cells
- Very limited reproductive toxicity data
- No data for immunotoxicity, developmental toxicity, chronic toxicity or carcinogenicity
- Structural analog benzotrichloride is established rodent carcinogen
  - No benzotrifluorides evaluated in chronic toxicity studies

Proposed Approach

Tier 1

- Conduct prechronic inhalation studies in rats and mice
  - Lack of prechronic inhalation toxicity studies in mice
  - Insufficient exposure concentrations in previous 13 week rat studies
  - Standard reproductive tissue histopathology and analysis of SMVC data will be included to determine the potential for reproductive toxicity
  - Include evaluation of the potential to induce alpha2μ-globulin nephropathy in male rats

Proposed Approach - Tiers 2 and 3

Tier 2

- Conduct 2-year toxicity and carcinogenicity studies in rats and mice
- Conduct a teratology study in rats
- Consider conducting a current guideline functional reproductive toxicology study in rats
  - Since these studies are typically conducted via the oral route, additional ADME/TK studies may be needed to relate exposures to those occurring by inhalation

Tier 3

- Consider conducting a perinatal toxicity study to evaluate effects on the developing reproductive, nervous and immune systems
  - Would require further information on exposure and use and consideration of the Tier 1 and Tier 2 study results

Questions and Comments